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Research article

The adjuvant use of plasma rich in growth factors in the inferior alveolar nerve repositioning technique

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ABSTRACT

Purpose: To describe the outcomes of the adjuvant use of plasma rich in growth factors (PRGF) in the inferior alveolar nerve repositioning surgery.
Material and methods: A retrospective report of three cases was conducted in a single private dental clinic. The variables were the residual alveolar bone height, the surgical complications, the occurrence of neurosensory complications, the marginal bone stability and the implant survival. A descriptive statistical analysis was performed.
Results: Three inferior alveolar repositioning were performed with the adjuvant use of PRGF. The residual alveolar bone height was 2.2 ± 0.14 mm. All patients underwent uneventful healing with no symptoms of neurosensory complications neither implant failure. The marginal bone loss was 0.1 ± 0.4 mm
Conclusions: The preventative and adjuvant use of PRGF in inferior alveolar nerve repositioning need to be assessed in prospective studies with a larger sample size.

1. Introduction

Several surgical techniques have been described to manage posterior mandibular atrophy prior to the rehabilitation with dental implants. The use of bone substitutes, onlay bone block grafting, distraction osteogenesis and short implants have been described [1, 2, 3, 4, 5, 6]. Transalveolar preparation of the cortical bone of the mandibular canal in association with extra-short implants has been also described to treat mandibular atrophy with a residual bone height of 3.5–5.0 mm [2]. However, when the residual alveolar bone height is less than 3 mm the primary stability of the short implants could be seriously compromised and other alternatives become necessary.

Repositioning of the inferior alveolar nerve is one surgical technique that allows the placement of dental implants in severely atrophied posterior mandible [7]. This technique requires clinical experience, detailed knowledge of the mandibular anatomy and the ability to deal with potential adverse events/complications [8]. It presents a high risk for sensory complications and may temporarily weaken the mandible (increasing the risk of mandible fracture) [8, 9]. In a systematic review, Vetromilla et al. have found neurosensory complications in 95.9% of the patients who received lateralization of the inferior alveolar nerve [8]. These complications have remained in 3.4% of the patients. Meanwhile, 58.9% of patients have shown neurosensory complications after IAN repositioning. This complication remained in 22.1%. For that, Dursun et al. have compared the short dental implants to the lateralization of the IAN and the placement of standard-length implants [10]. The risk/occurrence of complications has been higher in the standard implant group due to the lateralization of the IAN [10]. However, the marginal bone stability and implant survival have been comparable in both groups.

These outcomes would indicate the need to find ways to minimize the risk/occurrence of complications associated with IAN repositioning. The use of autologous plasma rich in growth factors has been described in the treatment of neuropathies with successful outcomes [11, 12, 13, 14, 15, 16, 17]. Several studies have indicated the neuroprotective, neurogenic, and neuroinflammatory modulator potentials of the autologous platelet rich plasma [14, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31].

The purpose of this study was to describe the outcomes of the use of plasma rich in growth factors in IAN repositioning technique to treat mandibular bone atrophy with a residual bone height of ≤3 mm. The specific aims of the study were: 1) to assess the surgical complications and the occurrence of neurosensory complications, and 2) to estimate the marginal bone stability and the implant survival rate.

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2. Materials and methods

2.1. Study design

To address the research purpose, the investigators designed and implemented a retrospective report of three cases. The study population was composed of all patients presented in a single dental clinic (Vitoria, Spain) for evaluating and management of vertical bone atrophy in the mandible between 2007 and 2018. To be included in the study sample, patients had to have dental implants placed in posterior mandible by the IAN repositioning technique. Otherwise, the patients were excluded. There were no specific exclusion criteria. This is a retrospective case report that is exempted from IRB approval. This study was performed following the Helsinki declaration regarding the investigation with human subjects and the patients gave their informed consent before the intervention.

Cone-beam CT scans (GALILEOS 3D, Sirona, USA) were analyzed with BTI scan software (Biotechnology Institute, Vitoria, Spain) to retrieve the distance from the residual alveolar crest to the mandibular canal and also to measure the bone density of the posterior mandible (Figure 1).

Patients received 2 g of amoxicillin and 1 g of acetaminophen 60 and 30 min before surgery, respectively. IV sedation and the local anesthesia were administered. Full thickness flap was then elevated. The implant site location was marked on the crestal surface with the initial drill working at high speed with irrigation. The cortical bone was then removed with piezoelectric inserts to uncover the inferior alveolar plexus. For IAN retraction a sterile glove was used. During the procedure the IAN was maintained wet with calcium-activated plasma rich in growth factors. Low speed biological drilling protocol at 150 rpm without irrigation was then employed following the manufacturer's protocol to prepare the implant site. After drilling, calcium-activated plasma rich in growth factors was injected into the implant site before the insertion of the dental implant. Fibrin membrane was then placed over the implant surface before the re-positioning of the IAN into the mandibular canal. PRGF clot was then placed over the IAN and the surgical site was covered by PRGF fibrin membrane (Figure 2). The flap was then repositioned and sutured with monfilament 5-0 Supramid® suture. The pos-operative care included the use of ice back during the first 2 h after surgery, antibiotic (amoxicillin 500 mg three times a day for one week) and analgesic (1 g of acetaminophen upon need). The patients were instructed not to wear the removal prosthesis and to follow a soft diet. Sutures were removed after 10 days of surgery. After 4–6 months of implant placement, trans-epithelial abutments (Multi-im, BTI Biotechnology institute) were connected to prepare screw-retained prostheses as described in previous publication [2].

2.2. Variables

The primary outcome was the occurrence of neurosensory complications as assessed by self-reported subjective sensory changes. The secondary outcomes were: 1) patients' demographic data (sex and age), 2) surgical complications. 3) the implant survival, defined as whether the implant was still in situ or had been removed. The cumulative dental implant survival rate was estimated by using time-to-event analyses (Kaplan-Meir method), and 4) the marginal bone loss defined as the increase in the distance between the uppermost point of the implant platform and the most coronal bone-implant contact. The reference value was this distance at the time of implant loading.

2.3. Data collection methods

Dental implants (BTI Biotechnology Institute, Vitoria, Spain) were followed clinically and radiographically to identify any sign of implant failure. The implant survival was positively evaluated if the implant was present at the last follow-up. The measurement of the marginal bone loss was performed on the most recent panoramic radiograph. The linear measurements was calibrated by the known implant length (Sidexis software, Sirona, USA). Follow-up visits after surgery were scheduled at 1, 7 and 14 days after surgery. Then at 1, 3, and 6 months. A visit was scheduled every 6 months thence after. Surgical complications, implant survival and marginal bone loss were monitored.

2.4. Statistical analysis

Data collection and analyses were performed by an independent examiner. Qualitative variable was described by the frequency analysis. Quantitative variables were described by the mean and standard deviation. Data analysis was performed with a statistical software package (SPSS).

3. Results

Three female patients were treated according to the described protocol where three IAN repositioning techniques were performed. The age of patient 1, patient 2 and patient 3 was 60, 63 and 70 years, respectively. At the implant second surgery, complete healing of the osteotomy sites could be observed (Figure 3). The residual alveolar bone height (coronal to the mandibular canal) was 2.2 ± 0.14 mm. The diameters and lengths of the three placed implants were 4.0 mm × 5.5 mm, 3.5 mm × 7.5 mm and 3.0 × 8.5 mm for patient 1, patient 2 and patient 3, respectively. The implants were placed at an insertion torque of 30 Ncm. All implants received delayed loading with screw-retained provisional prosthesis (Figure 3). The definitive prostheses were screw-retained partial fixed prosthesis (Figure 4). The follow-up time was 2, 4 and 5 years since the implant insertion, for patient 1, patient 2 and patient 3. The marginal bone loss was 0.1 ± 0.4 mm and no implant loss was registered. All patients underwent uneventful healing with no symptoms of neurosensory complications (Figure 5).

4. Discussion

With a residual alveolar bone height <3 mm, the inferior alveolar nerve repositioning and the immediate placement of short implants have

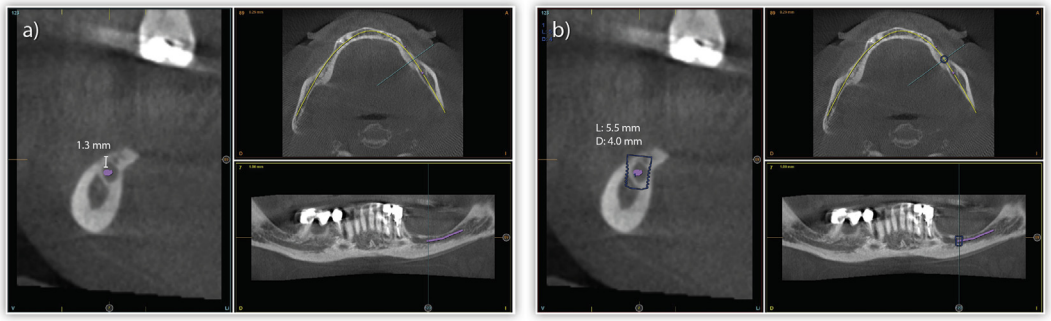

Figure 1. Preoperative cone-beam CT scan indicating severe mandiblar atrophy where 1.3 mm of alveolar bone are available coronal to mandibular canal.

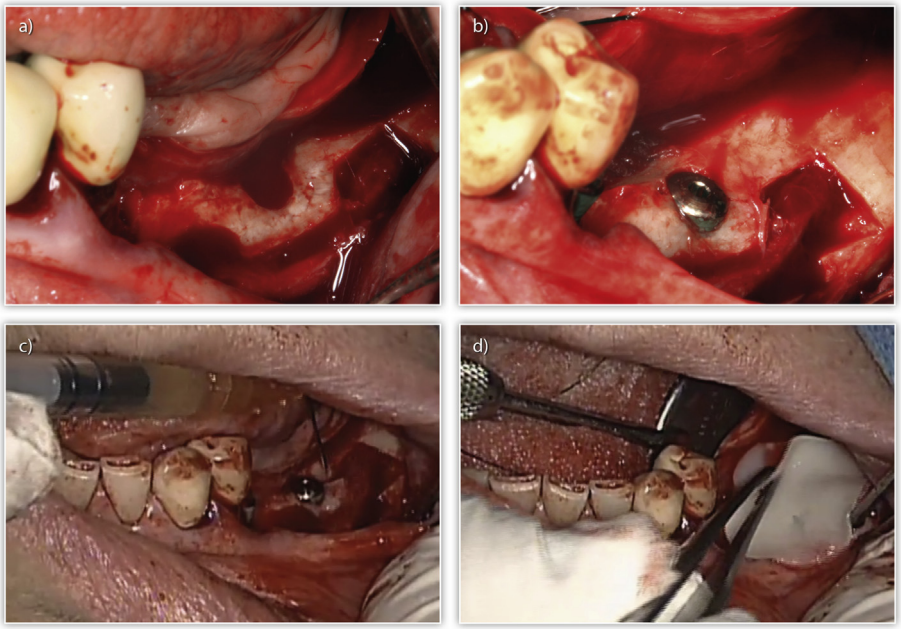

Figure 2. Inferior alveolar nerve (IAN) repositioning procedure. a: Implant site was marked before uncovering IAN. b) after completing implant insertion IAN was repositioned. c) Wetting IAN with activated liquid PRGF. d: Placement of PRGF membrane to cover the osteotomy and IAN before flap closure.

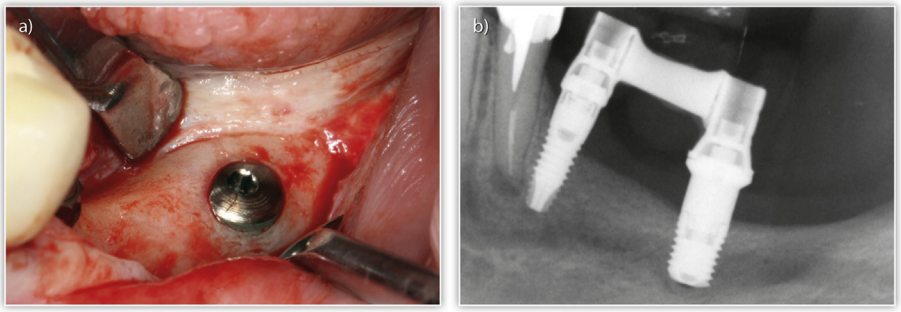

Figure 3. After 4 months of healing second implant surgery was performed. a: Complete bone healing at osteotomy site. b: Implant loading with screw-retained provisional prosthesis and placement of expanded transepithelial abutments on implant at second lower left molar position.

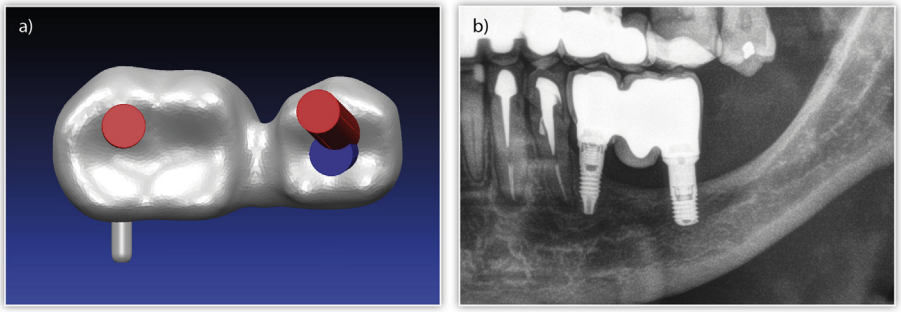

Figure 4. a: Design of metallic structure of definitive prosthesis with angulated screw channel restoration. b: Placement of definitive screw-retained prosthesis.

enabled the delivery of an implant-supported rehabilitation, with minimal post-operative events and discomfort.

The principal limitation of the IAN repositioning technique is the relatively high risk of neurosensory complications [8]. Several studies have indicated the neuroprotective, neurogenic, and neuroinflammatory modulator potentials of the autologous plasma rich in growth factor [11, 12, 23, 31]. This has a significant effect on the recovery of a functional nerve-muscle unit (both sensory and motor) [14, 18, 24]. Plasma rich in growth factors has been applied with successful outcomes in peripheral nerve injuries (PNIs) and neuropathies [13, 17]. It has been applied as a filler of nerve conduits or vein-muscle grafts across nerve gaps post trauma by Ultrasound-guided infiltrating the nerve stumps perineurally and intraneurally, or as scaffolds to bridge or wrap the injured nerve stumps [20, 21, 22, 25]. Moreover, there are non-traumatic peripheral

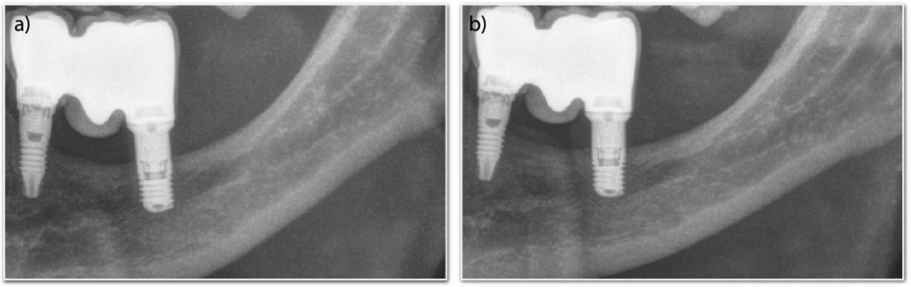

Figure 5. Radiographic follow-up of implant-retained prosthesis. a: after 12 months of implant insertion. b: after 54 months of implant insertion.

injuries such as compression, adhesion and fibrosis [19]. This approach may reduce undesirable consequences such as fibrotic scars and denervated organ atrophy; speeding up the functional recovery of the nerve-muscle unit [14, 17, 26, 27, 29, 30]. Therefore, plasma rich in growth factors may represent a synergistic adjunct to standard therapies in nerve regeneration and neuropathies.

It seems that the activity of autologous platelet rich plasma in preventing/treating nerve injury could be related to the modulation and the resolution of the inflammation, the activation of myelinating Schwann cells, macrophage polarization, and the activation of neo-angiogenesis [14, 17, 26, 27, 29, 30]. The use of plasma rich in growth factors would enable the modulation and resolution of the inflammatory process triggered by the implant site preparation and IAN manipulation.

Moreover, the type of autologous platelet concentrates may affect their potential in the regeneration of peripheral nerve healing. Torul et al. have compared the efficacy of PRGF and platelet rich fibrin (PRF) in the early period of healing of peripheral nerve injury [28]. The study concluded that the PRGF have increased the nerve regeneration while the PRF has a limited early action.

Dursun et al. have compared short dental implants to the lateralization of the IAN and the placement of standard implants [10]. The risk/occurrence of complications has been higher in the standard implant group due to the lateralization of the IAN [10]. However, the marginal bone stability and implant survival have been comparable in both groups. Extra-short implants (length $\leq$6.5 mm) are indicated when residual bone height is less than 7 mm and several studies are now available to support their indication for the treatment of severely atrophied residual ridges [1, 2, 3, 4, 5, 6]. For that, the use of short and extra-short implants (when is possible) could be more preferable option than the IAN repositioning technique.

This study has several limitations, the sample size, the absence of a control group, and the retrospective design. However, the data from this case report would encourage the conduct of a controlled prospective study to assess the adjuvant use of PRGF in a IAN repositioning techniques to reduce the rate of surgical and neurosensory complications.

5. Conclusions

The preventative and adjuvant use of PRGF in inferior alveolar nerve repositioning need to be assessed in prospective studies with a larger sample size.

Declarations

Author contribution statement

E. Anitua: conceived and designed the experiments; performed the experiments; contributed reagents, materials, analysis tools or data; wrote the paper.

M Alhraisat: conceived and designed the experiments; analyzed and interpreted the data; wrote the paper.

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Competing interest statement

The authors declare the following conflict of interests: Eduardo Anitua; is the Scientific Director of BTI Biotechnology Institute (Vitoria, Spain) and is the head of Eduardo Anitua Foundation, Vitoria, Spain. Mohammad Alkhraisat; is a researcher at BTI Biotechnology Institute (Vitoria, Spain).

Additional information

No additional information is available for this paper.

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